and R^5 is found in Example 48 (page 21), 58 (page 22), 81 (page 24), 44 (page 21), 67 (page 23), 69 (page 23), 57 (page 22), 72 (page 23), 73 (page 23) and 76 (page 24), respectively. Support for bromo and methyl within the definition of R^{13} is found in Examples 153 (page 31) and 174 (page 34), respectively.

REMARKS

Claims 1-8 and 10-17 are in this application. No claims are allowed. Claims 20-27 and Claims 9, 18, 19 and 28-31 are withdrawn from consideration as drawn to non-elected subject matter.

ELECTION OF SPECIES

The Examiner required the Applicants to elect one of the following three groups:

I. Claims 1-8 and 10-17 drawn to compounds of formula I, classified in various classes and subclasses;

II. Claims 20-27, drawn to a process, classified in various classes and subclasses; and

III. Claims 9, 18, 19 and 28-31, drawn to a method of use, classified in various classes and subclasses.

The Examiner further required the Applicants to elect a single disclosed species. The Applicants elected Group I and the species found on page 66, line 8, of the specification, namely naphthalene-2-carboxylic acid (6-guanidino-pyridin-3-yl)-amide. In a response dated October 12, 2001, the Applicants traversed the election of species requirement to the extent that the Examiner intended that the non-elected species would be permanently withdrawn from consideration.

The Applicants now have received a first office action making the above requirement final, wherein the Examiner stated "[c]laims 1-8 and 10-17 [of the elected Group I] are objected to as containing non-elected subject matter" and that "[t]his objection may be overcome by limiting the

claims to the elected subject matter identified supra." The Applicants request reconsideration for the following reasons.

The Applicants respectfully submit that there is no statutory, regulatory or procedural basis granting the U.S.P.T.O. the authority to object to a claim under examination on the basis that it contains non-elected subject matter in part. A claim is either in the application as encompassing elected subject matter or withdrawn from consideration as containing non-elected subject matter. If the elected claims encompass more than one species the Examiner may require that the Applicant elect a particular species for examination, but this a procedural tool and there is nothing found in the statutes, regulations or procedures which provide that the Applicant must amend the scope of a generic claim to excise non-elected species.

The Applicants direct the Examiner to 37 C.F.R. § 1.141 and the M.P.E.P. § 809.02(c)(B)(1), respectively:

§ 1.141

> "(a) Two or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed <u>in different claims</u> in one national application, provided that the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form (Section 1.75) or otherwise include all the limitations of the generic claim." (Emphasis added.)

§ 809.02(c)

> "An examiner's action subsequent to an election of species should include a complete action on the merits of all claims readable on the elected species."

> "(B) When a generic claim is subsequently found to be allowable, and not more than a reasonable number of additional species are claimed [in different claims], treatment shall be as follows:
>
> (1) When all claims to each of the additional species are embraced by an allowable generic claim as provided by 37 CFR 1.141, applicant must be advised of the allowable generic claim and that claims drawn to the nonelected species are no longer withdrawn since they are fully embraced by the allowed generic claim." (Emphasis added.)

The Applicants submit that the above sections from the Code and M.P.E.P. describe the proper procedures for restriction practice regarding genus and species claims. For the sake of clarity the Applicants point out the "a reasonable number" of species refers to those "specifically claimed" and not to the number of species embraced by the generic claim.

This is not an issue of whether one species is patentably distinct over another or whether a prior art reference anticipating one species would not render another obvious or whether it would be an undue burden to examine all claimed species. The issue here is whether the U.S.P.T.O. has the authority to force an applicant to divide up her or his generically claimed invention pursuant to an election of species requirement. The Applicants submit that the answer is an unequivocal no. In this regard, the Applicants respectfully direct the Examiner to the arguments made in their previous response.

The Examiner referred the Applicants to M.P.E.P. § 806.04(f), Claims Restricted to Species, by Mutually Exclusive Characteristics, in support of her position. Section 806.04(f) states, in part, that "[t]he general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, which a second claim recites limitations disclosed only for the second species and not the first." (Emphasis added.) Please note the plurality of "claims" in the above excerpt and the fact that the section is referring to restriction between species claims and not within a genus claim. The Applicants submit that Section 806.04(f) does not support the proposition that the Patent Office has the authority

under 35 U.S.C. § 121 to permanently withdraw non-elected species and compel an amendment narrowing the scope of an applicant's generically claimed invention. To the contrary, the Board of Patent Appeals and Interferences and its reviewing court have categorically held that Section 121 grants no such authority.

In this application, the Examiner goes further by drafting a claim for the Applicants. Hence, the Examiner, rather than the Applicants, defines the form in which the invention is claimed. The Applicants respectfully submit that such an action is improper. An applicant has a right to have each claim examined on the merits in the form she or he considers to best define her or his invention. It is not in the Examiner's purview to define the Applicant's invention for them.

After a "subgeneric concept, inclusive of the elected species " was "carved out" and presented to the Applicants, the Examiner withdrew the remaining subject matter of claims 1-8 and 10-17 and the subject matter of claims 9 and 18-31 from further consideration under the authority of 37 C.F.R. § 1.142(b). The Applicants respectfully point out that Section 1.142(b) provides that "[c]laims to the invention or inventions not elected, if not canceled, are nevertheless withdrawn from further consideration." (Emphasis added.) Please note that Section 1.142(b) refers to "claims" being withdrawn. Section 1.142(b) does not provide, however, that subject matter may be permanently withdrawn from a generic claim.

The Applicants have searched without success for some sort of statutory or judicial authority supporting the propriety of the Examiner's objection. To the contrary, the authority decisively indicates that the present objection to the Claims is improper. Accordingly, the Applicants submit that there is no basis for the objection to Claims 1-8 and 10-17 and respectfully request that the objection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112

The Examiner rejected Claim 1 for the terms "pharmaceutically acceptable salts" and "unnatural amino acid side chain" as indefinite. The Applicants have amended the former term in

accordance with the Examiner's suggested language and eliminated the latter term from the claim entirely. Accordingly, the Applicants believe that this rejection is overcome.

SUMMARY

In view of the foregoing, the Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Respectfully submitted,

6/24/02
Date

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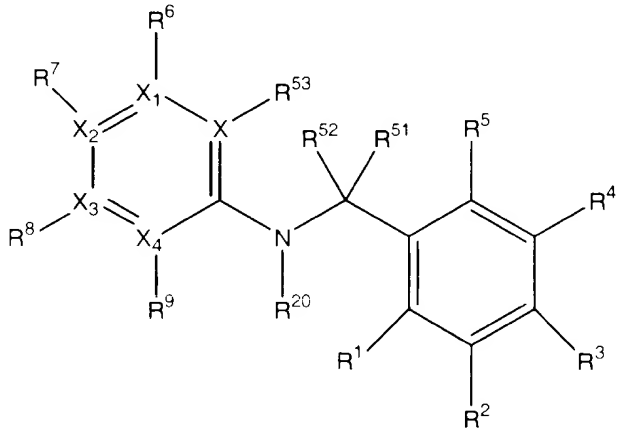
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims

Claim 1 has been amended as follows:

1. A compound of Formula I:



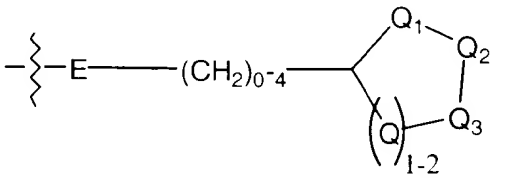
Formula I

its prodrug form or **a** pharmaceutically acceptable salt**[s]** thereof, wherein:

R^1 represents OH, COOH, COO-C_{1-4} alkyl, CH_2OR^{10}, SO_2-OH, O-SO_2-OH, O-SO_2-OC_{1-4} alkyl, $OP(O)(OH)_2$, or OPO_3C_{1-4} alkyl;

R^2, R^3, R^4, and R^5 independently at each occurrence represent H, SH, OR^{10}, halogen, $COOR^{10}$, $CONR^{11}R^{12}$, **[optionally substituted aryl,]** optionally substituted heterocyclyl, C_{4-14} cycloalkyl-C_{1-4} alkyl, C_{1-4} alkyl aryl, optionally substituted C_{1-14} straight chain, branched or cyclo alkyl, $NR^{10}R^{24}$, **4-carbamimidoylphenylazo, (2-morpholin-4-ylethylcarbamoyl)methoxy, 4-carbamimidoyl-phenylcarbamoyl, N=CH-N(CH_3)$_2$, 1,3-dioxo-1,3-dihydroisoindol-2-yl, toluene-4-sulfonylamino, 3-(4-carbamimidoylphenylcarbamoyl)-4-hydroxyphenylsulfanyl, O(CH_2)$_5$COOC_2H_5, O(CH_2)$_5$COOH,** $(CH_2)_{1-4}$-$NR^{33}R^{34}$, $(CH_2)_{1-4}$-$COOR^{33}$, O-$(CH_2)_{1-3}$-CO-het, O-$(CH_2)_{1-2}$-NH-CO-aryl, O-$(CH_2)_{0-2}$-NR^{10}-CO-$NR^{10}R^{33}$, O-$(CH_2)_{0-2}$-C(O)-$NR^{33}R^{34}$,

$O\text{-}(CH_2)_{1\text{-}4}\text{-}COOR^{10}$, $O\text{-}(CH_2)_{1\text{-}3}\text{-het-}R^{32}$, O-optionally substituted cycloalkyl, $O\text{-}(CH_2)_{1\text{-}4}\text{-}NR^{10}\text{-}COO\text{-}t\text{-butyl}$, $O\text{-}(CH_2)_{1\text{-}4}\text{-}NR^{10}R^{33}$, $O\text{-}(CH_2)_{1\text{-}4}\text{-}NR^{10}\text{-}C(O)\text{-}C_{0\text{-}3}$-alkyl-optionally substituted aryl, $O\text{-}(CH_2)_{0\text{-}6}$-optionally substituted aryl, $(CH_2)_{1\text{-}4}\text{-}NH\text{-}C(O)O\text{-}(CH_2)_{1\text{-}4}\text{-}PhR^{13}R^{14}$, NO_2, $O\text{-}(CH_2)_{0\text{-}4}\text{-}C(O)\text{-}NH$-tetrahydro carboline, SO_3H, $CH(OH)COOR^{10}$, $NR^{10}R^{28}$, $O\text{-}(CH_2)_{1\text{-}3}$-optionally substituted het, CH_2COOCH_3, $CH{=}CH\text{-}COOCH_3$,



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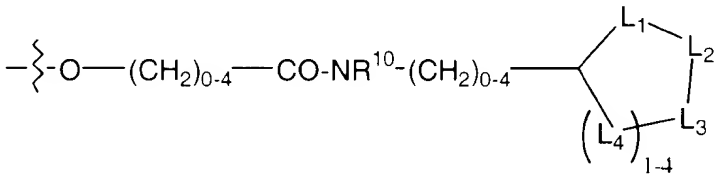
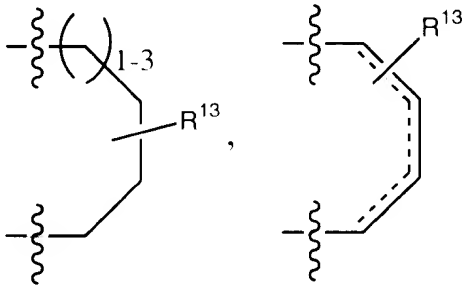


;

alternatively R^2 and R^3, R^3 and R^4, or R^4 and R^5 taken together form



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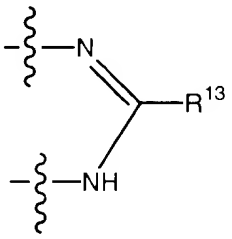

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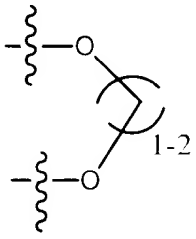
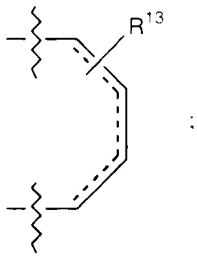


;

R^6, R^9 and R^{53} independently at each occurrence represents H, halogen, cyano, $C_{1\text{-}4}$ alkyl, $C_{1\text{-}4}$ halogenated alkyl, NO_2, O-aryl or OR^{11};

alternatively R^6 and R^{53} taken together form



;

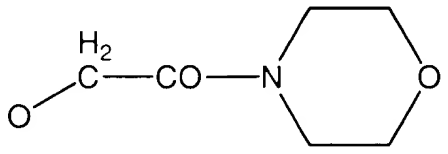
R^7 and R^8 independently at each occurrence represent OH, CF_3, H, COOH, NO_2, C_{1-4} alkyl, OC_{1-4} alkyl, **[or]**O-aryl, halogen, cyano, or a basic group selected from guanidino, $NH(CH=NH)NH_2$, $C(=NH)N(R^{10})_2$, C(=NH)-NH-NH_2, $C(=O)N(R^{10})_2$, 2-imidazoline, N-amidinomorpholine, N-amidino piperidine, 4-hydroxy-N-amidino piperidine, N-amidino pyrrolidine, tetrahydro pyrimidine, $C(O)CH_2NH_2$, $C(O)NHCH_2CN$, $NHCH_2CN$, and thiazolidin-3-yl-methylideneamine; with the proviso that only one of R^7 and R^8 represent a basic group;

R^{10} independently at each occurrence represents H, $(CH_2)_{0-2}$-aryl, C_{1-4} halo alkyl, or C_{1-14} straight chain, branched or cyclo alkyl, and alternatively, when one atom is substituted with two R^{10} groups, the atom along with the R^{10} groups can form a five to 10 membered ring structure;

X_1, X_2, X_3 and X_4 independently at each occurrence represent a carbon or a nitrogen atom;

R^{11} and R^{12} independently at each occurrence represent H or C_{1-4} alkyl;

R^{13} represents H, OH, **bromo, methyl,** OC_{1-4} alkyl, OAr, OC_{5-10} cycloalkyl, OCH_2CN, $O(CH_2)_{1-2}NH_2$, **[OCH_2COOH,]** OCH_2COO-C_{1-4} alkyl or



;

R^{20} represents H or OH;

R^{24} represents R^{10}, $(CH_2)_{1-4}$-optionally substituted aryl, $(CH_2)_{0-4}OR^{10}$, CO-$(CH_2)_{1-2}$-$N(R^{10})_2$, $CO(CH_2)_{1-4}$-OR^{10}, $(CH_2)_{1-4}$-$COOR^{10}$, $(CH_2)_{0-4}$-$N(R^{10})_2$, SO_2R^{10}, COR^{10}, $CON(R^{10})_2$, $(CH_2)_{0-4}$-aryl-$COOR^{10}$, $(CH_2)_{0-4}$-aryl-$N(R^{10})_2$, or $(CH_2)_{1-4}$-het-aryl;

R^{28} represents $(CH_2)_{1-2}$-Ph-O-$(CH_2)_{0-2}$-het-R^{30}, C(O)-het, CH_2-Ph-CH_2-het-$(R^{30})_{1-3}$; $(CH_2)_{1-4}$-cyclohexyl-R^{31}, CH_2-Ph-O-Ph-$(R^{30})_{1-2}$, CH_2-(CH_2OH)-het-R^{30}, CH_2-Ph-O-cycloalkyl-R^{31}, CH_2-het-C(O)-CH_2-het-R^{30}, or CH_2-Ph-O-(CH_2)-O-het-R^{30};

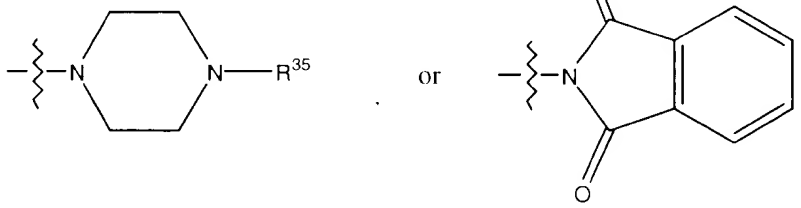
R^{30} represents $SO_2N(R^{10})_2$, H, NHOH, amidino, or $C(=NH)CH_3$;

R^{31} represents R^{30}, amino-amidino, NH-$C(=NH)CH_3$ or R^{10};

R^{32} represents H, C(O)-CH_2-NH_2, or C(O)-$CH(CH(CH_3)_2)$-NH_2;

R^{33} and R^{34} independently at each occurrence represent R^{10}, $(CH_2)_{0-4}$-Ar, optionally substituted aryl, $(CH_2)_{0-4}$ optionally substituted heteroaryl, $(CH_2)_{1-4}$-CN, $(CH_2)_{1-4}$-$N(R^{10})_2$, $(CH_2)_{1-4}$-OH, $(CH_2)_{1-4}$-SO_2-$N(R^{10})_2$;

alternatively, R^{33} and R^{34} along with the nitrogen atom that they are attached to forms a 4 to 14 atom ring structure selected from tetrahydro-1H-carboline; 6,7-Dialkoxyoxy-2-substituted 1,2,3,4-tetrahydro-isoquinoline,



R^{35} represents R^{10}, SO_2-R^{10}, COR^{10}, or $CONHR^{10}$;

E represents a bond, $S(O)_{0-2}$, O or NR^{10};

Q, Q^1, Q^2, Q^3, L^1, L^2, L^3 and L^4 independently at each occurrence represent N-natural **[or unnatural]** amino acid side chain, CHR^{10}, O, NH, $S(O)_{0-2}$, N-C(O)-NHR^{10}, SO_2-$N(R^{10})_2$, N-C(O)-NH-$(CH_2)_{1-4}$-R^{26}, NR^{10}, N-heteroaryl, N-C(=NH)-NHR^{10}, or N-$C(=NH)C_{1-4}$ alkyl;

R^{26} represents OH, NH_2, or SH;

R^{51} and R^{52} independently represent COOH, CH_2OH, CH_2COOH, COOR, CH_2COOR, alkyl or CO-NH_2; alternatively

R^{51} and R^{52} taken together represent =O, =S, $=CH_2$ or $=NR^{10}$;

R^{53} represents H, halogen, cyano, C_{1-4} alkyl, C_{1-4} halogenated alkyl, NO_2, O-aryl or OR^{11};

with the proviso that at least two of X_1, X_2, X_3 and X_4 represent a carbon atom, and when any of X_1, X_2, X_3 and X_4 represent a nitrogen atom the corresponding substituent does not exist.